SOLANDRINE, A NEW MIDRIATIC ALKALOID.

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Solandra lævis, from which this alkaloid was obtained, is a tropical evergreen shrub of the natural order Solanaceæ, tr. atropeæ, and is indigenous to South America and the West Indies. It grows plentifully in Australia, and used to be quite a common plant in suburban gardens, but of recent years has become scarce.

Attention was first drawn to the dangerous nature of the sap of Solandra by the following accident. A gardener who, while pruning, had some juice squirted into his eyes, was admitted to a hospital in Sydney suffering from loss of sight. It was found that his pupils were intensely dilated as if by atropine, and the effect was traced to Solandra growing in his garden.

The property of dilating the pupil of the eye is common to all the tropeines, but this very valuable action is accompanied by other objectionable properties which vary with the different members of the group, and this makes the discovery of a new member of special interest, in the hope that the deleterious qualities may be less or entirely absent.

The material for this investigation was kindly supplied by Mr. Maiden from plants growing in the Botanic Gardens, Sydney.

First, in order to obtain a general idea of the composition of the leaves, a complete proximate analysis was made by the method of Dragendorff.

The following tables show the constituents of the leaves :—

The fresh leaves—		
Water removed by air-drying		78·40 %
Water removed at 100° C.		2·145
Mineral constituents (ash)		3·125
Organic constituents (by difference)		16·33
		100·00
The air-dried leaves—		
Water at 100° C		9·93
Mineral constituents (ash)		14·46
Removed by solvents		34·34
Cellulose, lignin, etc. (by difference)		41·27
		100·00

The air-dried leaves contain :—

i. *Extracted by petroleum spirit*		3·692 %
Volatile oli	0·305 %	
Resins	0·257	
Chlorophyll	0·880	
Fixed oil	2·250	
ii. *Extracted by ether*		2·582 %
Fixed oil	1·211 %	
Water sol. portion	0·519	
Chlorophyll and resins	0·852	
iii. *Extracted with alcohol*		8·330 %
Glucose	trace.	
Saccharose	2·88 %	
Alkaloid	0·11	
Tannin	4·30	
Phlobaphene	1·04	
iv. *Extracted with water*		19·740 %
Mucilage	4·13 %	
Glucose	5·44	
Saccharose	4·71	
(Undetermined)	5·46	
		34·344 %

Extraction of the alkaloid.—In a preliminary trial on a small quantity of leaves, there was obtained evidence of the presence

of an exceedingly active and poisonous alkaloid. In order to obtain an amount sufficient for further investigation, 1000 grams of leaves were exhausted with boiling water faintly acidulated; the solution was evaporated to dryness, and its residue extracted with alcohol in a Soxhlet extractor. The alcoholic solution containing all the alkaloid was then distilled in vacuo, the residue dissolved in water, and the solution filtered. This clear aqueous solution was acidified with H_2SO_4, and shaken out, first with amyl alcohol, then with ether, till nothing further was removed. The residual aqueous solution was then rendered alkaline and shaken out with ether. On evaporation of the solvent 0·865 gram of impure alkaloid was obtained.

Purification.—The crude material was dissolved in slightly acid water and shaken with ether in alternately alkaline and acid solution; the ethereal layer was separated and the shaking out repeated till no further residue was observed on evaporating the solvent. The total ethereal extract now yielded 0·39 gram of alkaloid. The aqueous solution was further shaken out with chloroform, and from this, after removal of the solvent, was obtained a residue of 0·188 gram. This residue was found later to be non-alkaloidal.

It was noticed, when the solutions were warmed to volatilise the solvent, that a strong odour was evolved resembling that of nicotine or conine, and suggesting the admixture of a volatile alkaloid.

To test this point the ether residue (0·39 gram) was dissolved in acidulated water, then made faintly alkaline and distilled in a current of steam. The distillate was strongly alkaline; but when neutralised and evaporated to small bulk it gave negative results in every case on testing with all the ordinary alkaloid reagents. The same process was likewise gone through with the chloroform residue (0·188 gram) and again the distillate was found to be non-alkaloidal.

From this it may be definitely inferred that no volatile alkaloid is present, and that the distillate is strongly alkaline by ammonia formed probably from the amidenitrogen in the plant.

The liquid left in the retort from the first distillation contained the whole of the alkaloid, which was recovered by shaking out with chloroform, and now weighed 0·164 gram. This much purer material was used for the subsequent examination.

Chemical properties.—The material as obtained in the above manner is a yellow viscous mass, which becomes quite fluid on gently warming. It is quite free from odour, even on heating. The solubility in benzene and ether is slight; it is very soluble in chloroform and in alcohol; but slightly soluble in water, giving an alkaline solution and possessing a bitter taste. All attempts to crystallise it failed, hence the difficulty of its purification.

The aqueous solution gave well marked ppts. with the following alkaloid reagents:—I in KI, picric acid, phosphotungstic acid, tannic acid, $AuCl_3$, $PtCl_4$, and $KI.HgI_2$. In Vitali's test a bright purple colour was obtained.

Phenolphthalein is not reddened. $HgCl_2$ 5 % in alcohol, gives a white precipitate (atropine gives yellow, and red on warming). $PtCl_4$ gives, in a strong solution after standing some time, perfect yellow cubical crystals, which decompose at 170°C. $AuCl_3$ yields two kinds of crystals, transparent colourless cubes and octohedra, mixed with irregular yellow crystalline masses. With picric acid, radiating groups of prisms are obtained showing many curved and feathery crystals.

10 mgms. of the alkaloid were next hydrolysed with barium hydroxide, and on separation of the products of hydrolysis there were obtained, first, an acid which crystallised on evaporation in long thin needles having a melting point of 106°C; and secondly, a basic substance which resembled the original viscous yellow alkaloid in appearance, but formed a very different platinum salt. The quantity was not sufficient to decide whether the base is tropine or oscin. From 10 mgms. of the alkaloid were obtained by hydrolysis 35 % of an acid possessing the identical m. point and properties of atropic acid, and 30 % of an uncrystallisable base. This ratio of acid to base is equal to 1·17, which is the exact theoretical ratio of tropic acid to tropine in the well known atropine group.

Physiological properties.—Dr. H. G. Chapman has carried out for me a number of experiments on rabbits, frogs, and dogs. Introduced into a rabbit's eye, 0·1 mgm. of solandrine causes full dilatation of the pupil, with loss of the light reflex in twenty minutes. The inequality of the pupils may be noted until the fourth day after the instillation.

On the frog's heart solandrine possesses the property of paralysing the receptive substance for the endings of the vagus nerve. After the application of solandrine, stimulation of the trunk of the vagus no longer abolishes or interferes with the rhythm of the heart. Stimulation of the crescentic junction of auricle and sinus also fails to arrest the beat.

In the dog the injection of 8 mgms. of solandrine abolished the secretion of saliva and tears, accelerated the rate of respiration, increased the rate of the heart beat, and raised the blood pressure. Stimulation of the peripheral end of the divided vagus further failed to cause any alteration of the rhythm of the heart beat or the height of the blood pressure.

In these respects solandrine exhibits the action of the atropine group of nerve and muscle poisons.

Summary and Conclusions.—The alkaloid is proved to belong to the atropine group (1) By its chemical constitution: it splits up, on hydrolysis, into a base and an acid in precisely the same ratio as tropine to tropic acid in atropine and its isomers. (2) By its chemical and physiological properties: it gives Vitali's test in common with all the members of this group; it produces complete dilatation of the pupil, and all the effects characteristic of the natural tropeines on the heart, the secretory glands and the blood pressure.

It exhibits the following differences in properties from the well known tropeines :—phenolphthalein is not reddened by the solution; alcoholic solution of mercuric chloride causes a white ppt., atropine gives red, hyoscyamine gives yellow, and hyoscine a white ppt.; the platinum salt crystallises in small cubical crystals, whilst atropine is monoclinic, and hyoscyamine triclinic; the aurochloride crystals also are quite different.

Solandrine more closely resembles hyoscine. Both are thick syrups in the free state, yield white ppts. with alcoholic mercuric chloride, and form cubical platinic chlorides. It differs from hyoscine in its aurochloride, in not reddening phenolphthalein, and by the fact that it yields atropic instead of tropic acid when hydrolysed.

Though much still remains to be done in working out the exact constitution of the alkaloid, I consider that the above results afford sufficient evidence of the existence of a new tropeine alkaloid in *Solandra lævis*, for which, therefore, the name Solandrine is proposed.

I have to express my best thanks to Professor Anderson Stuart for the numerous facilities he has kindly afforded me in carrying out the above work in his laboratory.

Corrigendum.—I take the opportunity of drawing attention to a necessary correction in my paper on 'The Stinging Property of the Giant Nettle-tree' (These Proceedings, 1906, xxxi., p.530). In the table on p.536 the inorganic matter has been inadvertently included twice; the table should read as follows:—

	On fresh leaves.	On air-dried leaves.
Extracted by Petroleum spirit	0·60	2·56
Ether	0·33	1·41
Absolute alcohol	0·88	3·74
Water	2·47	10·60
Total extracted by solvents	4·28%	18·31%
Moisture by air-drying	76·65	
,, and vol. acids at 110° ...	3·11	13·30
Inorganic matter = ash	3·60	15·42
Cellulose, lignin (by difference)... ...	12·36	52·97
	100·00	100·00

Also on p.535, line 24, *for* 4·74% *read* 3·74%.